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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,670	12/14/2001	Agathe Subtil	216907US0X	4884

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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
FORD, VANESSA L	
ART UNIT	**PAPER NUMBER**
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/014,670	SUBTIL ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-10 and 39-47* is/are pending in the application.

4a) Of the above claim(s) *30-33 and 38-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-10,34-37 and 44-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. Applicant's response filed November 6, 2006 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Rejection Maintained

3. The rejection of claims 7-10, 34-37 and 44-47 under 35 U.S.C. 103(a), is maintained for the reasons set forth on pages 3-5, paragraph 4 of the Final Office Action.

The rejection is on the grounds that Demers et al teach a method of identifying polypeptides by: a) providing genes under the control of the type III secretion machinery, b) transcriptional fusion between the promoters of the type III genes and a reporter gene are constructed and introduced into wild-type gram-negative bacteria and mutants of these bacteria constitutively secrete proteins *via* the type III secretion machinery and c) the expression of the presence or activity of the protein product is demonstrated *via* the reporter gene (page 3). Demers et al teach that *Shigella* bacteria are gram-negative organisms that contain type III secretion machinery (page 1).

Demers et al do not teach *Chlamydia* polypeptides.

Graffais et al teach that *Chlamydia* polypeptides can be secreted by the type III secretion machinery and detected by techniques known in the art such as for example using cloning combined with vectors allowing expression of the Chlamydia polypeptides fused to markers (column 40).

Demers et al nor Graffais et al teach *Chlamydia* polypeptides selected from the group consisting of CPn0105, CPn0287, CPn0330, CPn0334 CPn374, CPn379, CPn705, CPn0710, CPn0711, CPn0820, CPn821, CPn1016 and CPn1022.

Kalman et al teach *Chlamydia* polypeptides from *Chlamydia pneumoniae* and *C. trachomatis* genomes (see the Title). Kalman et al teach for example, CPn0105 (CT016) which is a GcpE protein that is conserved in both the *Chlamydia pneumoniae* and *C. trachomatis* genomes (Table 1, page 5).

It would be *prima facie* obvious at the time the invention was made to identify polypeptides as taught by Kalman et al using the method of detecting polypeptides using Type III secretion machinery because Graffais et al teach that *Chlamydia*

polypeptides can be secreted by the type III secretion machinery and detected by techniques known in the art such as for example using cloning combined with vectors allowing expression of the *Chlamydia* polypeptides fused to markers as demonstrated by the teachings of Demers et al. Additionally, Kalman et al teach that comparative analysis of the *Chlamydia pneumoniae* and *C. trachomatis* genomes will significantly enhance the understanding of both pathogens and identification of genes shared between the two species supports the requirement for capabilities in biological systems that have, over long-term association with mammalian cells, evolved to reduce metabolic capacities while optimizing survival, growth and transmission of these unique pathogens (page 385). It would be expected barring evidence to the contrary that *Shigella* bacteria comprising type III secretion machinery would be effective in identifying *Chlamydia* secreted proteins.

Applicant's Arguments

Applicant urges that the claimed invention is an entirely different method of identifiying secreted *Chlamydia* proteins compared to what is described or suggested by the combination of prior art references. Applicant urges that Demers describe a method of screening for agents/compounds that change the expression of type III secretory proteins and/or which block secretion through this pathway. Applicant urges that Graffais describe a number of *Chlamydia* proteins some of which are characterized as Type III secreted proteins. Applicant urges that Graffais' teachings are not focused on this but rather disclose the genes and then goes on to describe that the genes and their corresponding proteins could be used for almost any imaginable use. Kalman et al is cited merely for the proposition that certain *Chlamydia* genes were known.

Applicant urges that one would not use Demers secretion system. Applicant urges that the cited art provides no reason to believe that the expression of *Chlamydia* proteins would work in other gram-negative strains such as *Shigella.* Applicant urges that there is no evidence that genes from such different organisms would be expressed nor would properly be secreted by the Type III machinery of that cell. Applicant urges

that heterologous secretion of secreted *Chlamydia* polypeptide can be obtained only if the signal of the *Chlamydia* polypeptide is identical to the signal of the bacteria in which the secretion is tested.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed November 6, 2006 have been fully considered but they are not persuasive.

It is the Examiner's position that the combination of references teach the claimed invention. One of ordinary skill in the art would be motivated to combine the prior art references because Demers et al teach a method of screening polypeptides using the type III secretion machinery of gram-negative bacteria. Applicant urges that Demers describes screening for agent/compounds that change the expression of type III secretory protein and/or which block secretion through this pathway. Graffais et al teach that *Chlamydia* polypeptides can be secreted by the type III secretion machinery and Kalman et al disclose the specific *Chlamydia* polypeptides that can be secreted by the type III secretion machinery of gram-negative bacteria. One of ordinary skill in the art would reasonably conclude that specific *Chlamydia* polypeptides can be identified by using the type III secretion machinery of gram-negative bacteria and that these polypeptides can be detected using techniques known in the art based on the combination of prior art references.

To address Applicant's comments regarding Demers et al, Demers et al teach screening or identifying compounds by the in use of gram-negative type III secretion

machinery (pages 2-3). The method steps include exposing the gram-negative bacterial cells to sample molecule wherein the bacterial cells contain a reporter gene transcriptionally fused to a promoter of gene activated or regulated by the type III secretion machinery and detecting the presence or activity of the product of the reporter gene.

To address Applicant's comments regarding compatibility of organisms or compatibility of type III machinery, Demers et al teach that any gram-negative bacteria containing type III secretion machinery may be used in the methods of this invention. Demer et al teach that suitable members of the of bacteria include *Shigella, Salmonella, Yersinia, Escherichia, Pseudomonas, Xanthomanas, Raistonia* and *Erwinia*. Based on the teaching of the prior art one of ordinary skill in the art would reasonably conclude that Chlamydia proteins can be secreted via the type III machinery of other gram negative organisms. Therefore, the type III machinery in these gram-negative organism is compatible.

To address the reference submitted by Applicant (Parsot, Tuckerdagger, Fields et al and Slepenkin et al), it should be noted that these references have been submitted to point out the necessity of coexpressing a chaperone protein to get secretion in *Salmonella* or the presence of functional chaperone protein *Chlamydia.* While it is true that chaperones play various roles in functions associated with the secretion of proteins it should be remembered that the method as disclosed in the combined teachings of the prior art would allow one of ordinary skill to identify secreted *Chlamydia* polypeptides via gram-negative type III machinery.

There is nothing on the record to show that the combination of teachings would not suggest the claimed invention.

3. The rejection of claims 7-10, 34-37 and 44-47 under 35 U.S.C. 103(a), is maintained for the reasons set forth on pages 5-6, paragraph 45of the Final Office Action.

The rejection was on the grounds that Stephens et al teach a method of identifying a secreted *Chlamydia polypeptide* comprising using a vector and transforming the cells into host cells (columns 15 and 16). Stephens et al teach that the vectors of the invention comprise the elements necessary to allow expression and/or secretion of nucleotide sequences in a host (column 16). Stephens et al teach that such bacteria host cell such as *E. coli* can be used for the expression of the proteins of the invention (column 16). Stephens et al teach that detection of *Chlamydia* gene expression can be performed in a variety of ways (column 15). Stephens et al teach a secreted protein, for example, CPn105 (CT016)(a polypeptide of the elected species) (see Table 2, columns 27-28).

Stephens et al do not teach the claim limitation "wherein said gram-negative strain containing a type III secretion pathway is a *Shigella* strain".

Demers et al teach that gram-negative bacteria contain type III secretion machinery and can secrete proteins via this machinery (pages 1 and 2). Demers et al teach that *Shigella* species can be used to secrete proteins (pages 1 and 6-9).

It would be *prima facie* obvious at the time the invention was made to modify the method of identifying *Chlamydia* polypeptides as taught by Stephens et al by using the Type III secretion machinery of Shigella to secrete a desired *Chlamydia* polypeptide because Demers et al has teach that polypeptides can expressed using the type III secretion pathway of gram-negative bacteria (e.g. *Shigella* species). It would be expected barring evidence to the contrary, that the type III secretion pathway of *Shigella* would be effective in secreting *Chlamydia* polypeptides.

Applicant's Arguments

Applicant urges that Stephens et al do not describe the expression of *Chlamydia* polypeptides in gram-negative bacterial strains containing a type III secretion pathway and the Examiner relies on Demers et al. Applicant urges that neither Stephens et al nor Demer et al describe a method for identifying secreted proteins but rather the

general methodology for expressing proteins. Applicant urges that Demers et al teach a method of screening polypeptides using the type III secretion machinery of gram-negative bacteria. Applicant urges that Demers describes screening for agent/compounds that change the expression of type III secretory protein and/or which block secretion through this pathway. Applicant urges that heterologous secretion of a secreted Chlamydia polypeptide is identical to the signal of the bacteria in which the secretion is tested and this not obvious for *Shigella* because the signal is still unknown and second because the phylogenic distance of Chlamydia with other organisms.

Examiner's Response to Applicant's Comments

To address Applicant's comments regarding Stephens et al, Stephens et al teach a method of identifying Chlamydia polypeptides but does not specifically teach that these polypeptides are identified using the type III secretion pathway of gram-negative bacteria. Thus, the Examiner relies on Demer et al to teach this claim limitation. Thus, the Examiner relies on the combination or reference to teach the claimed method.

To address Applicant's comments regarding Demers et al, Demers et al teach screening or identifying compounds by the in use of gram-negative type III secretion machinery (pages 2-3). The method steps include exposing the gram-negative bacterial cells to sample molecule wherein the bacterial cells contain a reporter gene transcriptionally fused to a promoter of gene activated or regulated by the type III secretion machinery and detecting the presence or activity of the product of the reporter gene.

To address Applicant's comments regarding compatibility of organisms or compatibility of type III machinery, Demers et al teach that any gram-negative bacteria containing type III secretion machinery may be used in the methods of this invention. Demer et al teach that suitable members of the of bacteria include *Shigella, Salmonella, Yersinia, Escherichia, Pseudomonas, Xanthomanas, Raistonia* and *Erwinia*. Based on the teaching of the prior art one of ordinary skill in the art would reasonably conclude that *Chlamydia* proteins can be secreted via the type III machinery of other gram negative organisms. Therefore, the type III machinery in these gram-negative organism is compatible regardless of the phylogenic distance of *Chlamydia* with other organisms.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Status of Claims

5. No claims allowed.

6. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew, can be reached at (571) 272-0787.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
January 16, 2006

NITA MINNIFIELD
PRIMARY EXAMINER